REMARKS

Interview Request

Applicants respectfully request a telephonic interview after the Examiner has reviewed the instant response and amendment. Applicants request the Examiner call Applicants' representative at 858 720 5133.

Status of the Claims

Pending claims

Claims 1 to 7, 9 to 12, 16, 17 and 28 to 54 are pending. Claims 34, 35, 38 are 44 have been withdrawn. Thus, claims 1 to 7, 9 to 12, 16, 17, 28 to 33, 36, 37 and 39 to 55 are pending and under consideration.

Outstanding Rejections

Claims 50 to 54 stand newly rejected under 35 U.S.C. §112, second paragraph. The rejection of claim 17 is maintained, and claims 50 to 54 are newly rejected, under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors at the time the application was filed had possession of the invention (written description requirement). The rejection of claims 1 to 7, 9 to 12, 17, 28 to 33, 36 and 37 is maintained, and claims 45 to 55 are newly rejected, under 35 U.S.C. §112, first paragraph, as allegedly not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention (enablement requirement). The rejection of claims 4 to 7, 11, 39 to 43, is maintained, and claims 1 to 3, 28 to 33, 36, 37, 45 and 51 to 55 are newly rejected, under 35 U.S.C. §102(b) as allegedly anticipated by Gelfand, et al., U.S. Patent No. 5,491,086.

Applicants respectfully traverse all outstanding objections to the specification and rejection of the claims.

sd-252049

Support for the Claim Amendments

The specification sets forth an extensive description of the invention in the new and amended claims in this and previous responses.

Claim Objections

The Patent Office had concerns regarding the grammatical structure of claims 9, 10, 12, 16, 17, 45 to 50 (see page 3, lines 1 to 9, of the instant office action ("the OA"). The instant amendment addresses this issue.

Issues under 35 U.S.C. §112, second paragraph

Claims 50 to 54 stand newly rejected under 35 U.S.C. §112, second paragraph. The Patent Office had concerns regarding reference to the "active site of the polymerase." The instant amendment addresses this issue.

Issues under 35 U.S.C. §112, first paragraph

Applicants respectfully request consideration of these remarks and reconsideration of Applicants' responses of September 17, 2004, and August 25, 2004.

Written Description

Claim 17

The rejection of claim 17 is maintained, and claims 50 to 54 are newly rejected, under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors at the time the application was filed had possession of the invention (written description requirement). In particular, it is alleged that the structural limitation is not sufficient enough to adequately describe the claimed genus's structure to function relationship.

Claim 17, as currently amended, is directed to isolated or recombinant nucleic acid encoding a polypeptide having polymerase activity, wherein the polypeptide has a sequence comprising at least 30 consecutive amino acids of a polypeptide having a

sequence as set forth in SEQ ID NO:2. Applicants respectfully submit that this claimed invention is sufficiently described in the specification such that one of ordinary skill in the art would have been able to ascertain the scope of the claims with reasonable clarity and recognize that Applicants' were in possession of the claimed invention at the time of filing.

The Federal Circuit has addressed the written description requirement in the context of biological sequences in Enzo Biochem. Inc. v. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . *i.e.*, complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.'" [Emphasis added] Id. at 1324, 63 USPQ2d at 1613. The court in Enzo adopted its standard from the USPTO's Written Description Examination Guidelines. See 296 F.3d at 1324, 63 USPQ2d at 1613 (citing the Guidelines). The Guidelines apply to proteins as well as DNAs. The Enzo court also stated:

> Similarly, in this court's most recent pronouncement, it noted:
>
> > More recently, in Enzo Biochem, we clarified that Eli Lilly did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure.

Amgen, 314 F.3d at 1332 [Amgen Inc. v. Hoechst Marion Roussel Inc., 314 F.3d 1313, 1330, 65 USPQ2d 1385, 1397 (Fed. Cir. 2003)]. Moba, B.V. v. Diamond Automation, Inc., 2003 U.S. App. LEXIS 6285; Fed. Cir. 01-1063, -1083, April 1, 2003.

Analogously, the structure of all of the species within the genus of nucleic acids encoding a polypeptide having polymerase activity, wherein the polypeptide has a sequence comprising at least 30 consecutive amino acids of a polypeptide having a sequence as set forth in

SEQ ID NO:2 (claim 17), are sufficiently correlated to a particular, known structure - in fact, they can only comprise a subsequence of SEQ ID NO:2; a physical property (at least 30 consecutive residues of SEQ ID NO:2); and, a function (polymerase activity). Accordingly, this genus of nucleic acids is defined via shared structural and functional properties in terms that convey with reasonable clarity to those skilled in the art that Applicants, as of the filing date and at the time of the invention, were in possession of the claimed invention.

The claimed subject matter need not be described in haec verba to satisfy the description requirement. It is not necessary that the application describe the claim limitations exactly, but only so clearly that one having ordinary skill in the pertinent art would recognize from the disclosure that applicants invented the claimed subject matter. In re Herschler, 591 F.2d 693, 700, 200 USPQ 711,717 (CCPA 1979). See also Purdue Pharma L.P. v. Faulding, Inc., 230 F.3d 1320, 1323, 56 USPQ2d 1481, 1483 (Fed. Cir. 2000) ("In order to satisfy the written description requirement, the disclosure as originally filed does not have to provide in haec verba support for the claimed subject matter at issue.").

Applicants respectfully aver that the specification describes the claim limitations sufficiently clearly that one having ordinary skill in the pertinent art would recognize from the disclosure that Applicants invented the claimed subject matter. The nucleic acids encoding a polypeptide having polymerase activity, wherein the polypeptide has a sequence comprising at least 30 consecutive amino acids of a polypeptide having a sequence as set forth in SEQ ID NO:2, are defined via shared physical and structural properties set forth in the specification in terms that convey with reasonable clarity to those skilled in the art that Applicants, as of the filing date and at the time of the invention, were in possession of the claimed invention. Accordingly, Applicants respectfully submit that the pending claims encompassing the claimed polymerase-encoding nucleic acids meet the written description requirement under 35 U.S.C. §112, first paragraph.

sd-252049

Claims 50 to 54

Regarding claims 50 to 54, it was alleged that the term "active site of a polymerase" and its use as a means of structurally describing the claimed polymerases was not supported by the specification at the time of filing, and the Patent Office requested Applicants indicate where support for this term can be found in the specification. Applicants respectfully aver that the specification describes the term "active site of a polymerase" sufficiently clearly that one having ordinary skill in the pertinent art would recognize from the disclosure that Applicants invented the claimed subject matter. For example, the paragraphs on pages 67, lines 9 to 20, and page 69, lines 23 to 27, expressly describe that the invention encompasses structural polypeptide motifs and functional polypeptide motifs such as, inter alia, enzymatic active sites, and describes a method for determining active site sequences (the following being an *in silico* method):

> Figure 5 is a flow diagram illustrating one embodiment of an identifier process 300 for detecting the presence of a feature in a sequence. The process 300 begins at a start state 302 and then moves to a state 304 wherein a first sequence that is to be checked for features is stored to a memory 115 in the computer system 100. The process 300 then moves to a state 306 wherein a database of sequence features is opened. Such a database would include a list of each feature's attributes along with the name of the feature. For example, a feature name could be "Initiation Codon" and the attribute would be "ATG". Another example would be the feature name "TAATAA Box" and the feature attribute would be "TAATAA". An example of such a database is produced by the University of Wisconsin Genetics Computer Group. Alternatively, the features may be structural polypeptide motifs such as alpha helices, beta sheets, or functional polypeptide motifs such as enzymatic active sites, helix-turn-helix motifs or other motifs known to those skilled in the art. [emphasis added]
>
> Motifs which may be detected using the above programs include sequences encoding leucine zippers, helix-turn-helix motifs, glycosylation sites, ubiquitination sites, alpha helices, and beta sheets, signal sequences encoding signal peptides which direct the secretion of the encoded proteins, sequences implicated in transcription regulation such as homeoboxes, acidic stretches, enzymatic active sites, substrate binding sites, and enzymatic cleavage sites. [emphasis added]

sd-252049

The specification also expressly describes assays that can determine fragments or variants of sequences of the invention which retain the enzymatic function, e.g., see page 53, lines 1 to 13:

> Another aspect of the invention is an assay for identifying fragments or variants of SEQ ID NO: 2, and sequences substantially identical thereto, which retain the enzymatic function of the polypeptides of SEQ ID NO: 2, and sequences substantially identical thereto. For example the fragments or variants of said polypeptides, may be used to catalyze biochemical reactions, which indicate that the fragment or variant retains the enzymatic activity of the polypeptides in the SEQ ID NO: 2.
>
> The assay for determining if fragments of variants retain the enzymatic activity of the polypeptides of SEQ ID NO: 2, and sequences substantially identical thereto includes the steps of; contacting the polypeptide fragment or variant with a substrate molecule under conditions which allow the polypeptide fragment or variant to function, and detecting either a decrease in the level of substrate or an increase in the level of the specific reaction product of the reaction between the polypeptide and substrate.

Applicants respectfully aver that the specification describes the claims directed to nucleic acids encoding polymerase active sites sufficiently clearly that one having ordinary skill in the pertinent art would recognize from the disclosure that Applicants invented the claimed subject matter. Accordingly, Applicants respectfully submit that the pending claims encompassing the claimed polymerase-encoding nucleic acids meet the written description requirement under 35 U.S.C. §112, first paragraph.

Enablement

The rejection of claims 1 to 7, 9 to 12, 17, 28 to 33, 36 and 37 is maintained, and claims 45 to 55 are newly rejected, under 35 U.S.C. §112, first paragraph, as allegedly not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention (enablement requirement).

The Patent Office states that the specification is enabling for the polynucleotide of SEQ ID NO:1, which encodes a polypeptide having polymerase activity.

However, it is alleged, inter alia, that the specification does not provide reasonable enablement for any nucleic acid comprising 85% sequence identity to SEQ ID NO:1, and encoding a polypeptide having polymerase activity, or, any nucleic acid encoding 30 consecutive amino acids of SEQ ID NO:2.

It appears the Patent Office's only remaining concern is that the claims may not be necessarily limited to nucleic acids encoding polymerases in which the complete nucleic acid has a specified structural relationship to either SEQ ID NO:1 or SEQ ID NO:2, because those claimed nucleic acids "comprise a sequence" which has a specified structural relationship to either SEQ ID NO:1 or SEQ ID NO:2 (see page 7, lines 1 to 5, and lines 12 to 17; and page 8, lines 1 to 12, of the OA). The Office referred to its 102 rejection, where it was alleged that the claimed nucleic acids need not themselves hybridize to SEQ ID NO:1, but merely "comprise a sequence" that will hybridize under the specified conditions to SEQ ID NO:1 (see page 10, lines 1 to 9, of the OA). The instant amendment addresses any possible ambiguity regarding this issue. For example, the claimed nucleic acid sequence itself must hybridize to SEQ ID NO:1 under the specified hybridization conditions. Additionally, the claims are limited to nucleic acids encoding polymerases in which the nucleic acid has a specified structural relationship to either SEQ ID NO:1 or SEQ ID NO:2.

It appears the Office is concerned that the "comprise a sequence" phrase includes sequences not enabled by the specification. However, Applicants wish to clarify that they use the terms "comprises" or "comprising" as open-ended terms. The transitional terms "comprising" and "comprises" (and other comparable terms, e.g., "containing," and "including") are "open-ended" - they cover the expressly recited subject matter, alone or in combination with unrecited subject matter. See, e.g., Genentech, Inc. v. Chiron Corp., 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997) ("'Comprising' is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim."); Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948) ("comprising" leaves the "claim open for the inclusion of unspecified ingredients even in major amounts"). See also MPEP §

2111.03. MPEP §2163, section II.A.1., page 2100-169, Rev. 2, May 2004. Applicants need not enable or describe "unrecited subject matter" as encompassed by the term "comprising". It is inappropriate for the Office to require Applicants to enable or describe "unrecited subject matter" as encompassed by the term of art "comprising" to satisfy the requirement of section 112.

Applicants respectfully aver that the specification enabled the skilled artisan at the time of the invention to identify, and make and use, a genus of polymerases and the nucleic acids that encode them to practice the claimed invention. The specification provides reasonable enablement to make and use the genus of claimed polymerase-encoding polynucleotides. Applicants need not enable or describe "unrecited subject matter" as encompassed by the term of art "comprising". Accordingly, the pending claims are sufficiently enabled by the specification to meet the requirements of 35 U.S.C. §112, first paragraph.

In light of these remarks, and the remarks from Applicants' previous responses, Applicants respectfully submit that the pending claims are fully enabled by and sufficiently described in the specification to meet the requirements of 35 U.S.C. §112, first paragraph.

Issues under 35 U.S.C. §102

Gelfand, et al., U.S. Patent No. 5,491,086

The rejection of claims 4 to 7, 11, 39 to 43, is maintained, and claims 1 to 3, 28 to 33, 36, 37, 45 and 51 to 55 are newly rejected, under 35 U.S.C. §102(b) as allegedly anticipated by Gelfand, et al., U.S. Patent No. 5,491,086 ("Gefland").

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987); MPEP § 2131.

The Patent Office expressed a concern regarding use of the phrase "a sequence" in reference to SEQ ID NO:1, because this phrase may be interpreted as if there exist multiple sequences with the result being that SEQ ID NO:1 comprises many different, contiguous and

overlapping sequences. The Office suggested use of "the sequence of SEQ ID NO:1" as opposed to "a sequence" of SEQ ID NO:1. The instant amendment addresses this issue.

As confirmed by Applicants, and noted by the Office, Gelfand teaches a nucleic acid having only 66.5% sequence identity to SEQ ID NO:1. Thus, because claim 1 (as currently amended) is directed to isolated or recombinant nucleic acids comprising a consecutive sequence having at least 85% sequence identity to the sequence of SEQ ID NO:1 and encoding a polypeptide having polymerase activity, or, sequences fully complementary thereto, Gelfand is not a single prior art reference that expressly or inherently describes each and every element of the claim. Thus, claim 1 cannot be anticipated by Gelfand.

Similarly, because claim 51 (as currently amended) is directed to an isolated or recombinant nucleic acid that encodes a polymerase, wherein the polymerase comprises a sequence that is a variant of SEQ ID NO:2, and the variant polymerase sequence has at least 85% sequence identity to SEQ ID NO:2, Gelfand is not a single prior art reference that expressly or inherently describes each and every element of the claim. Thus, claim 51 cannot be anticipated by Gelfand.

Because claim 52 (as currently amended) is directed to an isolated or recombinant nucleic acid that encodes a polymerase, wherein the polymerase comprises a sequence that is a variant of SEQ ID NO:2, and the variant polymerase sequence has at least 85% sequence identity to at least 200 consecutive residues of a polypeptide having a sequence as set forth in SEQ ID NO:2, and the sequence variation of SEQ ID NO:2 is not at the active site of the polymerase encoded by the nucleic acid, Gelfand is not a single prior art reference that expressly or inherently describes each and every element of the claim. Thus, claim 52 cannot be anticipated by Gelfand.

Because claim 54 (as currently amended) is directed to an isolated or recombinant nucleic acid that encodes a polymerase, wherein the polymerase comprises a sequence that is a variant of SEQ ID NO:2, and the variant polymerase sequence has at

least 70% sequence identity to at least 200 consecutive residues of a polypeptide having a sequence as set forth in SEQ ID NO:2, and the sequence variation at the active site of the polymerase encoded by the nucleic acid has at least 95% sequence identity to the active site sequence of SEQ ID NO:2, Gelfand is not a single prior art reference that expressly or inherently describes each and every element of the claim. Thus, claim 54 cannot be anticipated by Gelfand.

The Patent Office also alleged that the claimed nucleic acids need not themselves hybridize to SEQ ID NO:1, but merely "comprise a sequence" that will hybridize under the specified conditions to SEQ ID NO:1. The instant amendment addresses any possible ambiguity regarding this issue. The claimed nucleic acid sequence itself must hybridize to SEQ ID NO:1 under the specified hybridization conditions.

Applicants wish to clarify that they use the terms "comprises" or "comprising" as open-ended terms. The transitional terms "comprising" and "comprises" (and other comparable terms, e.g., "containing," and "including") are "open-ended" - they cover the expressly recited subject matter, alone or in combination with unrecited subject matter. See, e.g., Genentech, Inc. v. Chiron Corp., 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997) ("'Comprising' is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim."); Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948) ("comprising" leaves the "claim open for the inclusion of unspecified ingredients even in major amounts"). See also MPEP § 2111.03. MPEP §2163, section II.A.1., page 2100-169, Rev. 2, May 2004. It is inappropriate for the Office to speculate that unrecited subject matter as encompassed by the term of art "comprising" could render a claim anticipated.

Claim 4 (as currently amended) is directed to an isolated or recombinant nucleic acid encoding a polypeptide having polymerase activity, wherein the nucleic acid comprises (a) a consecutive sequence that hybridizes to a nucleic acid encoding a polypeptide having polymerase activity, wherein the nucleic acid hybridizes to the sequence as set forth in SEQ ID NO:1, under

hybridization conditions comprising about 42°C in 50% formamide, 5X SSPE, 0.3% SDS, and 200 ng/ml sheared and denatured salmon sperm DNA, and a wash step comprising a wash at 30 minutes at room temperature in a solution comprising 150 mM NaCl, 20 mM Tris hydrochloride, pH 7.8, 1 mM Na_2EDTA, 0.5% SDS, followed by a 30 minute wash in fresh solution, or, (b) a sequence fully complementary to (a). The nucleic acid taught by Gelfand, which is 66.5% identical to the exemplary SEQ ID NO:1, will not hybridize under these expressly specified conditions to SEQ ID NO:1. Thus, Gelfand is not a single prior art reference that expressly or inherently describes each and every element of the claim, and claim 4 cannot be anticipated by Gelfand.

Claim 5 (as currently amended) is directed to an isolated or recombinant nucleic acid encoding a polypeptide having polymerase activity, wherein the nucleic acid comprises (a) a consecutive sequence that hybridizes to a nucleic acid encoding a polypeptide having polymerase activity, wherein the nucleic acid hybridizes to the sequence as set forth in SEQ ID NO:1, under hybridization conditions comprising about 35°C in 35% formamide, 5X SSPE, 0.3% SDS, and 200 ng/ml sheared and denatured salmon sperm DNA, and a wash in a buffer comprising 0.1X SSC, 0.5% SDS for 15 to 30 minutes at between the hybridization temperature and 68°C, and a wash step comprising a wash at 30 minutes at room temperature in a solution comprising 150 mM NaCl, 20 mM Tris hydrochloride, pH 7.8, 1 mM Na_2EDTA, 0.5% SDS, followed by a 30 minute wash in fresh solution, or, (b) a sequence fully complementary to (a). The nucleic acid taught by Gelfand will not hybridize under these expressly specified conditions to SEQ ID NO:1. Thus, Gelfand is not a single prior art reference that expressly or inherently describes each and every element of the claim, and claim 5 cannot be anticipated by Gelfand.

Claim 45 (as currently amended) is directed to an isolated or recombinant nucleic acid encoding a polypeptide having polymerase activity, wherein the nucleic acid comprises (a) a consecutive sequence that hybridizes to a nucleic acid having the sequence as set forth in SEQ ID NO:1, across the entire length of SEQ ID NO:1, under hybridization conditions comprising about 42°C in 50% formamide, 5X SSPE, 0.3% SDS, and 200 ng/ml sheared and denatured salmon sperm DNA, and a wash step comprising a wash at 30 minutes at room temperature in a solution

comprising 150 mM NaCl, 20 mM Tris hydrochloride, pH 7.8, 1 mM Na_2EDTA, 0.5% SDS, followed by a 30 minute wash in fresh solution, or, (b) a sequence fully complementary to (a). The nucleic acid taught by Gelfand will not hybridize under these expressly specified conditions to SEQ ID NO:1. Thus, Gelfand is not a single prior art reference that expressly or inherently describes each and every element of the claim, and claim 45 cannot be anticipated by Gelfand.

Claim 53 (as currently amended) is directed to an isolated or recombinant nucleic acid that encodes a polymerase, wherein the polymerase comprises a sequence that is a variant of SEQ ID NO:2, and the variant polymerase sequence is encoded by a nucleic acid that hybridizes under stringent conditions to SEQ ID NO:1, and the sequence variation of SEQ ID NO:2 is not at the active site of the polymerase encoded by the nucleic acid, wherein the stringent hybridization conditions comprise a wash step comprising a wash at 30 minutes at room temperature in a solution comprising 150 mM NaCl, 20 mM Tris hydrochloride, pH 7.8, 1 mM Na_2EDTA, 0.5% SDS, followed by a 30 minute wash in fresh solution. The nucleic acid taught by Gelfand, which is 66.5% identical to the exemplary SEQ ID NO:1, will not hybridize under these expressly specified conditions to SEQ ID NO:1. Thus, Gelfand is not a single prior art reference that expressly or inherently describes each and every element of the claim, and claim 53 cannot be anticipated by Gelfand.

Applicants respectfully submit that the instant amendment and these remarks sufficiently addresses all of the Patent Office's concerns regarding Gelfand and claimed invention. Thus, the rejection under section 102(b) can be properly withdrawn.

sd-252049

CONCLUSION

In view of the foregoing amendment and remarks, Applicants respectfully aver that the Examiner can properly withdraw the rejection of the pending claims under 35 U.S.C. §112, first and second paragraphs and 35 U.S.C. §102(b). Applicants respectfully submit that all claims pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Applicants believe that no additional fees are necessitated by the present response and amendment. However, in the event any such fees are due, the Commissioner is hereby authorized to charge any such fees to Deposit Account No. 13-1952 referencing docket no. 564462001613. Please credit any overpayment to this account.

After the Examiner has reviewed this supplementary response and amendment, if the Examiner believes a telephonic interview would help expedite prosecution, please call Applicants' representative at (858) 720-5133.

Dated: March 28, 2005

Respectfully submitted,

By

Gregory P. Einhorn
Registration No.: 38,440
MORRISON & FOERSTER LLP
3811 Valley Centre Drive
Suite 500
San Diego, California 92130-2332
(858) 720-5133

sd-252049